Regulation of skeletal muscle mass *in vivo* in humans

**Outline**

- To provide an overview of the regulation of muscle mass after anabolic stimuli, and how it is assessed *in vivo* in humans

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"Exercise is king. Nutrition is queen. Put them together and you've got a kingdom."

-Jack Lalanne
Skeletal muscle plasticity
In vivo human research: Muscle reconditioning

Lance Armstrong

Jay Cutler
In vivo human research: Muscle de-conditioning

- sarcopenia
- obesity
- chronic kidney disease
In vivo human research: Lifestyle changes
Main anabolic stimuli to human muscle
Nutrition as an anabolic stimulus

Whole food sources of protein

Isolated proteins
Amino acids

‘Building blocks’

‘Anabolic signals’
Leucine is an anabolic signaling molecule.
Physical activity as an anabolic stimulus
Interaction between exercise and dietary protein on muscles

Synthesis of net ‘new’ proteins
Why is skeletal muscle important?
1. Locomotion
2. Muscle strength/performance
3. Regulation of blood glucose
4. Regulation of blood lipids
5. Largest reservoir of bodily amino acids
6. BMR
Daily muscle protein turnover

1-2% per day
(0.04 – 0.14 %·h⁻¹)

Or

300 – 600 g of muscle protein per 24 h

~2.5 to 5 lbs of lean meat
• Provide a single meal/exercise response of skeletal muscle reconditioning
  ✓ Repair
  ✓ Remodeling (muscle quality)
  ✓ Protein maintenance
  ✓ Protein accretion

• Primary variable dictating muscle net protein balance (MPS-MPB) in ‘healthy’ adults

• Long-term interventions are necessary to confirm the acute practice
Regulation of skeletal muscle mass

**Tools**
- Metabolic tracers
- Muscle Biopsies, breath, and blood collections
- Western blot readouts
- Intrinsically labeled food protein

**Endpoints**
- Digestion and absorption
- Whole body protein turnover
- Muscle protein synthesis
Meal factors that influence the building of muscle proteins after we eat...

- protein digestion and absorption
- splanchnic AA extraction
- plasma amino acid availability
- hormonal responses
- postprandial perfusion
- muscle AA uptake
- signaling proteins in muscle tissue
- muscle protein synthesis

Intrinsically labeled food protein

Gorissen S. thesis (2016)
Metabolic labeling from animal to human

- Stable isotope amino acid tracer
  - $^{[13C]}$leu & $^{[2H_5]}$phe
  - $^{[5,5,5-2H_3]}$leu

Prof. Carl Parsons and the Poultry Research Farm
Certain populations are ‘anabolically resistant’ to the main anabolic stimuli to muscles.
Increase adiposity blunts the ability of muscles to build ‘new’ muscle proteins after a meal.

Beals JW (2016) AJCN
Obesity diminishes the ability of muscles to build ‘new’ muscle proteins after a workout.

Protein digestion and absorption is severely impaired in hemodialysis patients. Post-meal amino acid availability:

- MHD patients: 41±5%
- Age- and BMI-matched controls: 61±5%

Van Vliet (2018) KI Reports
The muscles of hemodialysis patients are overstimulated and anabolic resistant.
“If exercise could be packed in a pill, it would be the single most widely prescribed and beneficial medicine in the nation.”

- Robert N. Butler, M.D.
Exercise factors that influence post-workout protein renewal and repair

- Exercise mode (e.g., weightlifting vs. endurance)

- Exercise intensity (e.g., %1RM or %VO₂peak)

- Exercise duration and volume
A single bout of weight lifting before protein ingestion enhances muscle protein synthesis versus eating alone for at least 1 day.

Meal: 15 g whey protein isolate

It doesn’t ‘work’ as well after running

1 hour at 70% VO$_{2}$peak, meal: 18 g protein, 17 g fat, & 60 g carbohydrate

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*S. Abou Sawan et al. (2018) Physiol Reports*
Nutritional factors that influence post-meal protein renewal and repair

- Whole foods vs. protein supplements
- Protein amount
- Meal frequency
- Cooking method
Food first approach to protein intake
Eating the whole egg stimulates a greater post-work muscle building response versus egg whites.
What’s in the whole egg?

**PROTEIN**
- ~5g protein per egg
- High biological value protein
- Stimulates skeletal MPS rates
- 20g of protein may maximally stimulate MPS without excess AA oxidation

**LIPIDS**
- ~4g fat per egg
- Cholesterol may stimulate mTORC1, thus influencing MPS
- Dietary cholesterol does not negatively impact blood cholesterol profiles
- Phospholipids with antioxidative function

**BIOACTIVE COMPOUNDS**
- Choline for acetylcholine synthesis and cell membrane integrity
- Antioxidants (Vitamins A, E; Selenium)
- Peptide efficacy in humans remains unclear

The **food matrix** describes the overall physical form of food, and includes how various food components are structured and their interactions.
How is this accomplished?

- Multidisciplinary research team consisting of medical professionals and scientists
  - Scott Paluska, MD, Christie Clinic
  - Ken Wilund, PhD, KCH
  - Carl Parsons, PhD, Poultry Research Farm
  - Anna Dilger, PhD, Meat Science Laboratory
  - Lucas Li, PhD & Alex Ulanov, PhD, Metabolomics Center
  - And many more…. 
• Human research can be challenging, but it is essential for the translational process.

• Exercise of all sorts will help us age gracefully and prevent disease; however, weight lifting regimens are really good for our muscles.

• Nutrients do not always act independently of each other and synergism is possible—this has implications to promote transition from single nutrient to food based guidelines.

• A food first approach will help optimize protein in the diet and prevent nutrient shortfalls, otherwise the yolk’s on you.